UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
11/212,109	08/26/2005	Jacques Dumas	BAYER-0052	5925

23599 7590 11/28/2016

MILLEN, WHITE, ZELANO & BRANIGAN, P.C.
2200 CLARENDON BLVD.
SUITE 1400
ARLINGTON, VA 22201

EXAMINER
SZNAIDMAN, MARCOS L

ART UNIT	PAPER NUMBER
1628	

NOTIFICATION DATE	DELIVERY MODE
11/28/2016	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

docketing@mwzb.com

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte JACQUES DUMAS, PAUL EHRLICH, and SUSANNE ZULEGER

Appeal 2014-008008
Application 11/212,109
Technology Center 1600

Before DONALD E. ADAMS, DEMETRA J. MILLS, and JOHN E. SCHNEIDER, *Administrative Patent Judges*.

MILLS, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134. The Examiner has rejected the claims for obviousness-type double patenting. We have jurisdiction under 35 U.S.C. § 6(b).

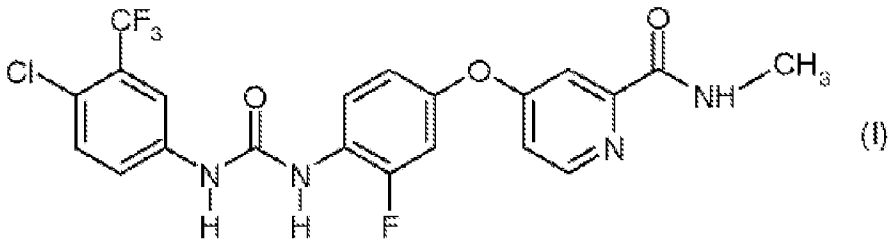
WE AFFIRM.

STATEMENT OF CASE

The following claim is representative.

1. A composition comprising:

a) 4{4-[3-(4-chloro-3-trifluoromethylphenyl)-ureido]-3-fluorophenoxy}-pyridine-2-carboxylic acid methyl amide of Formula I



(I)

and/or salts, hydrates., or solvates thereof, and b)

a pharmaceutically acceptable matrix agent in the form of a solid dispersion, wherein the pharmaceutically acceptable matrix agent comprises at least one polymer which is polyvinylpyrrolidone, copovidone, vinylpyrrolidone/ vinylacetate copolymer, crospovidone, polyalkylene glycol, including polyethylene glycol ; polyethylenoxide, poloxamer, hydroxyalkyl cellulose, including hydroxypropyl cellulose; hydroxyalkyl methyl cellulose, including hydroxypropyl methyl cellulose; carboxymethyl cellulose, sodium carboxymethyl cellulose, ethyl cellulose, cellulose succinates, cellulose phthalates, polymethacrylates, polyhydroxyalkylacrylates, polyhydroxyalkylmethacrylates, polyacrylates, polyvinyl alcohol, polyvinyl acetate, vinyl alcohol/vinyl acetate copolymer, xanthan gum, galactomannanes, carrageenan, chitosan, chitin, alginic acid, salts of algininc acid, polylactides, dextrins, starch, starch derivatives, proteins or polyethylene oxide.

App. Br. 14 (Claims Appendix).

Cited References

Riegelman et al.	US 4,151,273	Apr. 24, 1979
Nakamichi et al.	US 5,456,923	Oct. 10, 1995
Aoki	US 2003/0099703 Al	May 29, 2003
Appel	US 2003/0224043 Al	Dec. 4, 2003
Juppo	US 2004/0067256 Al	Apr. 8, 2004
Boyer et al.	US 8,637,553 B2	Jan. 28, 2014
Hirose et al.	EP 1275386 A1	Jan. 15, 2003
Bateman et al.	WO 03/043630 A1	May 30, 2003

Abu T. M. Serajuddim, *Solid Dispersion of Poorly Water-Soluble Drugs: Early Promises, Subsequent Problems, and Recent Breakthroughs*, Vol. 88 No. 10 J. PHARMACEUTICAL SCIENCES 1058–66 (1999).

Christian Leuner and Jennifer Dressman, *Improving drug solubility for oral delivery using solid dispersions*, 50 EUROPEAN J. PHARMACEUTICS AND BIOPHARMACEUTICS 47–60 (2000).

Grounds of Rejection

Claims 1, 3–22 and 36–45[1] stand provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1–6, 9–11 and 56–58 of copending Application No. 10/895,985 (now US 8,637,553 to Boyer et al. (hereinafter, Boyer)), in view of Leuner, Serajuddim, Aoki, Juppo, Bateman, Appel, Hirose, Nakamichi and Riegelman.

FINDINGS OF FACT

The Examiner's findings of fact are set forth in the Answer at pages 3–9 and Final Act., pages 4-8.

---

[1] Claims 25, 46 and 47 have been withdrawn from consideration by the Examiner as directed to a non-elected invention. Ans. 3.

PRINCIPLES OF LAW

In making our determination, we apply the preponderance of the evidence standard. *See, e.g., Ethicon, Inc. v. Quigg*, 849 F.2d 1422, 1427 (Fed. Cir. 1988) (explaining the general evidentiary standard for proceedings before the Office).

Obviousness-type double patenting entails a two-step analysis. First, the allegedly conflicting claims are construed and, second, the difference(s) between the claims are considered to determine whether the claims are patentably distinct. *See, Eli Lilly & Co. v. Barr Labs., Inc.,* 251 F.3d 955, 968, (Fed. Cir. 2001). "A later patent claim is not patentably distinct from an earlier patent claim if the later claim is obvious over, or anticipated by, the earlier claim." *Id.*

> All proper double patenting rejections, of either type, rest on the fact that a patent has been *issued* and later issuance of a second patent will continue protection, beyond the date of expiration of the first patent, of the very same invention claimed therein (same invention type double patenting) or of a mere variation of that invention which would have been obvious to those of ordinary skill in the relevant art (obviousness-type double patenting). In the latter case, there must be some clear evidence to establish why the variation would have been obvious which can properly qualify as "prior art."

In re Kaplan, 789 F.2d 1574, 1579–80 (Fed. Cir. 1986) (emphasis in original).

Obviousness-type Double Patenting

We agree with the Examiner's fact finding, statement of the rejection and responses to Appellants' arguments as set forth in the Answer. We find

that the Examiner has provided evidence to support a prima facie case of obviousness-type double patenting. We provide the following additional comment to the Examiner's argument set forth in the Final Rejection and Answer. The application in question has matured into the Boyer patent, therefore, the provisional nature of the rejection is withdrawn and we treat the rejection as an obviousness-type double patenting rejection.

Appellants admit that, "Claims 1-5, and 56, and 58 of U.S. Application No. 10/895,985, which issued as claims 1-5 and 13 and 15 of US Patent No. 8,637,553, are directed the compound of formula I and salts thereof." App. Br. 4. Appellants argue that

> The subject matter of the claims herein are directed to solid dispersions with specific pharmaceutically acceptable matrix agents which are not obvious variants of the broad generic subject matter defined by the claims in Application No. 10/895,985, which issued as US Patent No. 8,637,553. There is no evidence or allegation the claims of Application No. 10/895,985 and US Patent No. 8,637,5536, provide direction that would lead one skilled in the art to the solid dispersions claimed herein with the matrix agents specified. There is also no evidence it would be obvious to try to form the solid dispersions claimed from this broad generic disclosure.

App. Br. 5. Appellants further argue that

> There is no evidence showing the secondary references teach that the preparation of solid dispersions is routine and can be formed with all active compounds, as suggested in the advisory action. There is also no evidence the secondary references provide direction in how to predict which pharmaceuticals will form solid dispersions or which will provide advantages as solid dispersions. There is also no evidence the solid dispersions formed by the secondary references contain compounds which are analogous to the compounds of formula I and salts thereof. One secondary reference, Hirose, is cited for disclosing solid dispersions of compounds with some structural features of the compound of formula I but these compounds are so structurally

> distinct, there is no allegation or suggestion they are analogous to the compound of formula I.

App. Br. 6. We are not persuaded. There is no question that Boyer teaches the claimed compound of formula I. App. Br. 4; Final Act 4. The Examiner cites the remaining references to show that,

> the prior art teaches that solid dispersion formulations are commonly used in the pharmaceutical industry in order to improve the solubility and/or bioavailability of a large and diverse structural and biological type of drugs.
>
> At the time of the invention it would have been prima facie obvious for a person of ordinary skill in the art to make a solid dispersion of known active agents including the fluoro compound of formula I disclosed in application # 0/895,985 in order to obtain a better formulation with better oral bioavailability, thus resulting in the practice of claims 1, 3-22 and 36-47 with a reasonable expectation of success.

Final Act. 7.

While Appellants argue that there is no evidence showing that the secondary references teach that the preparation of solid dispersions is routine and can be formed with varying active compounds, we disagree. Leuner teaches the advantages of using solid dispersions to address solubility issues associated with drugs. Abstract. Aoki teaches that the creation of a solid dispersion is of interest to improve the solubility of a slightly soluble medicament, for example, nifedipine, phenytoin, nitrofurantoin, benoxaprofen, griseofulvin, sulfathiazole, tacrolimus, piroxicam, carbamazepine, phenacetin and cyclic GMP phosphodiesterase inhibitors. ¶¶ 4 and 8. "Juppo teaches a solid dispersion formulation of felodipine and bicatulamide (*see* paragraphs [0033] and [0034])." Final Act 6.

> Appel teaches solid dispersion formulation for an enormous variety of drugs (see paragraph [0035]. Further, Appeal teaches that the drug does not need to be a low solubility drug in order to benefit from the invention, although low solubility drugs represent a preferred class for use with the invention (see paragraph [0026]). Hirose teaches solid dispersion formulations of compounds of formula I (see page 2), la (page 4) and lb (page 5) which show some of the structural features of compound I, like ureas and substituted pyridine rings, etc. Nakamichi teaches new methods for producing solid dispersions (see abstract) which includes the use of polyvinylpyrrolidone (see column 2, line 49-50) as one of the preferred polymers, an teaches an enormous variety of drugs which include: antipyretic, analgesic, anti-inflammatory, antiulcer, coronary vasodilators, antibiotics, antimicrobials, antispasmodic, bronchodilators, diuretics, etc, (see column 3, line 50 through column 5, line 48).
>
> Finally, Riegelman teaches solid dispersion formulations in general. In summary, the prior art teaches that solid dispersion formulations are commonly used in the pharmaceutical industry in order to improve the solubility and/or bioavailability of a large and diverse structural and biological type of drugs.

Final Act. 6–7. Appel also teaches that that one class of drugs that will benefit from solid dispersion formulations, are drugs with a clogP value of at least 3.0 and preferable 4.0, a clogP which the Examiner alleges is similar to that of the compound of formula I. Ans. 12-13, 18. The Examiner has provided evidence to support a prima facie case of obviousness-type double patenting and evidence that those of ordinary skill in the art at the time of the present invention were able to routinely prepare diverse drugs in the form of solid dispersions, and that the prior art suggest that compounds having similar properties to the compound of formula I would benefit from being prepared as a solid dispersion.

Appellants argue that Leuner discloses dosing limitations and manufacturing concerns when preparing solid dispersions. App. Br. 7-8. Reply Br. 6-7. Appellants further argue that Craig[2] and other of the cited references also disclose manufacturing concerns and poor predictability of solid dispersion behavior. App. Br. 10, Reply Br. 8-30. We have weighed these disclosures against the multitude of successful preparations of solid dispersions disclosed in the cited prior art using PVP, and have found that the balance of the evidence supports the Examiner's conclusion that the preparation of solid dispersions using PVP is routine. We further agree with the Examiner that Craig does not specifically disclose why numerous solid dispersion which have been published never made it to market, and that they may not have made it to market for reasons unrelated to the fact that they are solid dispersions. Ans. 27.

The Appellants argue that, "the examples of the application illustrate that these two polymers [polyvinylpyrrolidone (PVP) and hydroxypropyl cellulose] provide solid dispersions which are effective drug delivery systems for the compound of formula I. The compound of formula I is shown to be highly soluble in both polymers." App. Br. 11. Appellants argue that the examples in the Specification provide evidence of unexpected results. *Id.* More particularly, Appellants argue that

> Tables 1 and 2 on pages 26 and 27 of the application show significant improvements in bioavailability in animal models using a solid dispersion of this invention with polyvinylpyrrolidone over

---

[2] Craig, et al., "The mechanisms of drug release from solid dispersions in water-soluble polymers," International Journal of Pharmaceutics, 231, (2002) p 131-144.

> conventional formulations of a free base of a compound of formula I and pharmaceutically acceptable salts of a compound of formula I.

App. Br. 12.

We have carefully reviewed Appellants' proffered evidence of unexpected results obtained from a formulation comprising a compound of formula I, PVP, and crosscarmellose in accordance with Example 11 of the Specification, as provided in Table 2 of the Specification, page 27, but are not persuaded by it. Appellants' evidence does not show that the improved bioavailability results were unexpected in view of the disclosures Luener, Seradjuddim, Aoki, Bateman, Appel, Hirose, Nakamichi and Riegelman. Expected beneficial results are not evidence of nonobviousness. *See In re Skoner*, 517 F.2d 947, 950 (CCPA 1975). Each of the cited references show that the preparation of a pharmaceutical agent in the form of a solid dispersion improves the solubility and bioavailability of the pharmaceutical agent, and that it is beneficial that the formulation include PVP. Ans. 12-17.

Moreover, Appellants' evidence of unexpected results is not commensurate in scope with the claims. The claims are not limited to a solid dispersion of a compound of formula I, PVP, and crosscarmellose[3]. "It is well established that the objective evidence of nonobviousness must be commensurate in scope with the claims." *In re Lindner*, 457 F.2d 506, 508 (CCPA 1972). Furthermore, unexpected results must be between the claimed invention and the closest prior art." *In re Fenn*, 639 F.2d 762, 765 (CCPA 1981). Hirose, cited by the Examiner, shows a compound with some

---

[3] Crosscarmellose is cross-linked carboxymethylcellulose. https://en.wikipedia.org/wiki/Croscarmellose_sodium

of the structural features of compound 1 prepared as a solid dispersion including hydroxyl propyl cellulose (HPC), and polyvinyl pyrrolidone (PVP) (see paragraph [0024]). Ans. 7-8. Appellants provide no evidence of unexpected results in view of the closest prior art, including compounds such as that of Hirose. Claims 7-10, 12-16, 43 and 44 fall for the reasons of record and for the same reasons as claim 1.

The obviousness-type double patenting rejection is affirmed for the reasons of record.

CONCLUSION OF LAW

On balance we finds that the preponderance of the evidence of record supports the Examiner's obviousness-type double patent rejection, which is affirmed for the reasons of record.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED